

Amendments to the Specification:

Please replace the title of the application ("USE OF THE MK FAMILY AS HEMATOPOIETIC FACTORS") on page 1, line 2, with the following amended title:

--EXPANSION OF HEMATOPOIETIC CELLS USING MIDKINE OR  
PLEIOTROPHIN--

Please replace the paragraph beginning at page 13, line 3, with the following amended paragraph:

--Next, using a hematopoietic stem cell assay medium, complete type (Lot No. 96101601; Kyokuto Seiyaku Kogyo) containing IL-3, SCF, G-CSF, and EPO, the colony assay was carried out with peripheral blood cells from a healthy normal individual. This assay is considered to be performed under conditions closer to *in vivo*. Results with MK are shown in Figures 12 and 13, and those with PTN in Figures 14 and 15. No increase in BFU-E was observed with any combinations including MK + IL-3, MK + SCF, and MK + G-CSF. However, the combinations of MK + EPO and PTN + EPO were assumed to increase BFU-E. Erythroblast precursor cells, BFU-E, were formed on the 14th day of culture, and are known to be more undifferentiated than CFU-E formed on the 5th to 7th days. Addition of MK or PTN to a Kyokuto complete medium resulted in formation of at the highest 2 or more times as many BFU-E as the complete medium alone on the 12th day after the initiation of culture. These results indicate that at least the addition of MK to the complete medium results in promoting the proliferation of erythroblasts as well. As described above, it is evident that the MK family is capable of acting on hematopoietic stem cells and hematopoietic precursor cells in the hematopoietic tissues of mammals to maintain, proliferate, and differentiate them, and synergistically or additionally enhancing the above-described functions by the combined use with various cytokines such as SCF, M-CSF, G-CSF, GM-CSF, IL-3 AND IL-6. Especially, the MK family remarkably promotes the proliferation of CFU-Mix, which is very close to multipotential stem cells, under conditions closer to *in vivo*. The MK family also promotes the proliferation and differentiation of granulocyte/macrophage precursor cells and exerts the

remarkable neutrophil increasing effect in an *in vivo* neutropenia model. This MK family alone or in combination with more than one cytokine including SCF, M-CSF, G-CSF, GM-CSF, IL-3, and IL-6 can be clinically applied and, especially, used for the *ex vivo* expansion of hematopoietic stem cells in the transplantation of bone marrow and stem cells derived from the peripheral blood and umbilical cord blood. In addition, the MK family is expected to be used for the treatment of patients with and prevention of neutropenia, ~~[[vertebrate]]~~ refractory anemia, and leukemia caused by cancer chemotherapy. Furthermore, the MK family would be used in the future for proliferating stem cells for gene therapy targeting hematopoietic stem cells. Especially, it is very promising to increase the dose density in cancer chemotherapy by the combined use of MK with G-CSF, improving effects of chemotherapy by increasing the dose of antitumor drugs or shortening the administration period.--

Please replace the paragraph beginning at page 15, line 1, with the following amended paragraph:

--Figures 2A and 2B ~~[[illustrates]]~~ illustrate effects of single or combined use of MK, G-CSF, GM-CSF, M-CSF, IL-3, IL-6 and SCF on G colony, GM colony and M colony-forming capabilities of mononuclear cells in human peripheral blood different from that used in the experiment in Figure 1.--

Please replace the paragraph beginning at page 15, line 6, with the following amended paragraph:

--Figures 3A and 3B ~~[[illustrates]]~~ illustrate numbers of granulocytes, monocytes, or macrophages, and other cells counted by the esterase double staining of human peripheral blood mononuclear cells after two-week liquid-culture in the presence of MK, G-CSF, GM-CSF, IL-3, IL-6, and SCF alone or in combination.--

Please replace the paragraph beginning at page 22, line 8, with the following amended paragraph:

--The MK family acts on hematopoietic stem cells and precursor cells of various hemocytes of hematopoietic tissues of mammals to maintain, proliferate, and differentiate them. Furthermore, the above-described functions are synergistically or additionally enhanced by the combined use of MK with other cytokines such as SCF, M-CSF, G-CSF, GM-CSF, IL-3, and IL-6. Especially, the MK family exerts remarkable proliferation promoting effects on CFU-Mix, which is very close to multipotential stem cells, under conditions closer to *in vivo*. The MK family also promotes the proliferation and differentiation of precursor cells of the granulocytes/macrophages and remarkably increase neutrophils in neutropenia *in vivo*. The pharmaceutical composition of the present invention containing the MK family alone, or containing the MK family in combination with one or more cytokines such as SCF, M-CSF, G-CSF, GM-CSF, IL-3, and IL-6 can be clinically applied, especially, to the *ex vivo* expansion of stem cells in the transplantation of bone marrow and stem cells derived from the peripheral blood and umbilical cord blood. The MK family is also expected to be used for treating and preventing neutropenia, [[inveterate]] refractory anemia, and leukemia caused by the cancer chemotherapy. Furthermore, the MK family is expected to be used for the stem cell proliferation for gene therapy targeting hematopoietic stem cells.--